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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
AM101333

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Signature _____

Typed or printed name _____

Application Number	Filed
10/796,925	March 10, 2004

First Named Inventor
Wumin LI

Art Unit	Examiner
1645	Lakia J. Tongue

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☑ attorney or agent of record.
Registration number 50,437.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

Frank R. Cottingham
Signature

Frank R. Cottingham
Typed or printed name

973 660 7660
Telephone number

Mar. 31, 2009
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re of Application of:	Wumin LI, et al.		
Application No.:	10/796,925	Group Art No.:	1645
Filed:	March 10, 2004	Examiner:	Tongue, Lakia J.
For:	ADJUVANTED BOVINE VACCINES		
Confirmation No.:	3270		
Customer Number:	25291		

Mail Stop AF
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW -- ATTACHMENT

Dear Commissioner:

Applicants respectfully request a review of the outstanding rejections made against the claims in the above-captioned patent application. Applicants believe that the outstanding rejections are clearly improper due to the omission of essential elements required to establish a *prima facie* rejection. This Request is being submitted concurrently with a Notice of Appeal and the corresponding Notice of Appeal filing fee.

A. Summary of Claimed Subject Matter

The present claims are directed to vaccination methods involving the use of a vaccine composition comprising inactivated or killed whole *E. coli* O157:H7, an adjuvant and aluminum hydroxide. The adjuvant is defined in claim 22 as being an oil emulsion comprising:

(a) 1% to 3% vol/vol of polyoxyethylene-polyoxypropylene block copolymer;

(b) 2% to 6% vol/vol of squalane;

(c) 0.1% to 0.5% vol/vol of polyoxyethylene sorbitan monooleate; and

(d) buffered salt solution.

Thus, the currently claimed invention requires, *inter alia*: (i) a precisely defined oil emulsion adjuvant; and (ii) a combination of the oil emulsion adjuvant with aluminum hydroxide.

B. Errors in the Rejection

The claims were rejected under 35 U.S.C. § 103 as being unpatentable over Johnson *et al.* ("Johnson"), Saito *et al.*, U.S. 2005/0158330 ("Saito"), and Baylor *et al.* (2002) *Vaccine 20*:S18-S23 ("Baylor"), and further in view of Elder *et al.* (2002) *J. Animal Sci. 80*:151, abstract 602 ("Elder").

The rejections are clearly erroneous because not all elements of the claims are taught or suggested in the cited art. In particular, the cited art fails to teach or suggest an oil emulsion adjuvant as defined in claim 22. In addition, the cited art fails to teach or suggest the combination of an oil emulsion adjuvant with aluminum hydroxide. Furthermore, the Examiner has not presented a reasonable explanation as to why a person of ordinary skill in the art would have been motivated to combine or modify the cited art in a manner that would result in a method that falls within the scope of Applicants' claims.

1. The Cited Art Does Not Teach or Suggest an Oil Emulsion Adjuvant as Defined in the Present Claims

The Examiner has relied on Saito as allegedly teaching the oil emulsion adjuvant of the present claims. According to the Examiner:

> Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), non-ionic surfactants, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene polyoxypropylene glycol and the like.

(Office Action dated January 7, 2008, page 5, lines 17-21). The Examiner cited to paragraph 0034 of Saito to support this statement. Paragraph 0034 of Saito, however, lists ten different possible surfactant emulsifiers. The Examiner has not even attempted to explain why a person of ordinary skill in the art would have been motivated to select from this list of ten items the precise components that are recited in Applicants' claims. Moreover, nothing in Saito teaches or suggests combining polyoxyethylene-polyoxypropylene block copolymer with polyoxyethylene sorbitan monooleate. Again, the Examiner has not made any attempt to explain why this particular combination of ingredients would have been obvious.

In addition, no explanation has been put forth to explain why a skilled person would have been motivated to combine polyoxyethylene-polyoxypropylene block copolymer or polyoxyethylene sorbitan monooleate with squalane and a buffered salt solution. In fact, squalane is only

mentioned in Saito in paragraph 0028 as one of fifteen possible "non-ester oil base[s]." The Examiner has not explained why a skilled person would have specifically selected squalane from this list.

When one considers the extremely large number of combinations of ingredients that are possible based on the multiple laundry lists of ingredients recited in Saito, it is very hard to fathom why a skilled person would have been motivated to specifically arrive at the combination of: polyoxyethylene-polyoxypropylene block copolymer + squalane + polyoxyethylene sorbitan monooleate + buffered salt solution, as required by the present claims. The Examiner has not explained why this particular combination would have been obvious.

Not only does Saito fail to teach the specific combination of ingredients of the oil emulsion adjuvant of the present claims, but Saito also fails to teach the recited percentages of these ingredients. There is no logical or scientifically sound reason that would explain why a skilled person would have arrived at 1% to 3% of polyoxyethylene-polyoxypropylene block copolymer, 2% to 6% of squalane and 0.1% to 0.6% of polyoxyethylene sorbitan monooleate. Thus, it was erroneous for the Examiner to completely disregard the percentages recited in the claims for purposes of assessing non-obviousness.

2. The Cited Art Does Not Teach or Suggest Combining an Oil Emulsion Adjuvant with Aluminum Hydroxide

None of the cited references teach or suggest the combination of an oil emulsion adjuvant and aluminum hydroxide. In fact, a skilled person, in view of the cited art, would have been discouraged from making such a combination. For instance, aluminum hydroxide is disclosed in Saito solely as a comparative control adjuvant and there is nothing to suggest combining aluminum hydroxide with an oil emulsion adjuvant. Moreover, the examples in Saito show that aluminum hydroxide adjuvanted formulations performed significantly worse than oil emulsion formulations. (*See* Applicants' Reply dated October 14, 2008, page 3, line 26 – page 5, line 2). Baylor also teaches against the use of aluminum hydroxide by emphasizing the negative aspects of this component such as "local reactions, production of IgE antibodies, and the inability to elicit cell-mediated immunity." (*See* Applicants' Reply dated October 14, 2008, page 5, lines 3-14). These teachings would have further discouraged a person of ordinary skill in the art from using aluminum hydroxide in combination with an oil emulsion vaccine formulation.

The Examiner has not presented any logical or scientifically sound reasons as to why a skilled person would have been motivated to combine an oil emulsion adjuvant with aluminum hydroxide. Instead, the Examiner simply asserted that:

> Saito does not specifically disclose the combination of components, however it would have been obvious to one of ordinary skill in the art to combine the components together along with aluminum hydroxide because aluminum hydroxide is a known adjuvant that is well known in the art to stimulate an immune response.

(Office Action dated January 7, 2009, page 6, lines 11-15). The mere fact that aluminum hydroxide is a known adjuvant that stimulates an immune response is insufficient to explain why a skilled person would have been motivated to use aluminum hydroxide in combination with an oil emulsion adjuvant -- much less the specific oil emulsion adjuvant defined in the present claims. Furthermore, the Examiner has failed to acknowledge or address the negative aspects of aluminum hydroxide that are reported in Saito and Baylor.

C. Summary and Conclusions

The Examiner has repeatedly cited to the Supreme Court case of *KSR International v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) in an attempt to justify the rejections. The Examiner, however, has failed to acknowledge or appreciate the Court's emphasis on assessing *predictability* in obviousness inquiries. *Id.* at 1739. Where a combination of elements does not result in a predictable outcome, a finding of obviousness is inappropriate under *KSR*. For example, in the recent case of *Sanofi-Synthelabo v. Apotex*, 550 F.3d 1075 (CAFC 2008), the Federal Circuit affirmed the district court's finding of non-obviousness in an unpredictable field (chemistry) based in part on the "wide range of possible outcomes" that the prior art would have presented to a person of ordinary skill in the art. *Id.* at 1089. Significantly, in the present case, the Examiner has not addressed the predictability of combining the individual elements of the cited references whatsoever. Indeed, the chemical arts in general, and the art of adjuvant formulation in particular, are not regarded as inherently predictable, and no evidence to the contrary has been made of record. Thus, a proper application of *KSR* to the present claims strongly supports Applicants' position of non-obviousness.

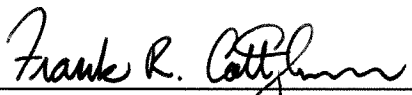
Applicants have previously presented a careful analysis of the exemplary rationales for obviousness that are set forth in MPEP § 2143. Applicants' analysis clearly showed that none

of the exemplary rationales can apply to the currently claimed invention. (*See* Applicants' Reply filed on June 19, 2008, page 6, line 1, through page 7, line 13). The Examiner has not addressed these rationales and has not presented any alternative rationales that would justify the obviousness rejections.

The Supreme Court in its *KSR* Opinion emphasized the well established proposition that "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* at 1741 (citing *In re Kahn*, 441 F.3d 977 (2006)). Here, Applicants submit that the Examiner has attempted to make out an obviousness rejection on mere conclusory statements without any articulated reasoning or rational underpinning to support the rejection.

In view of the foregoing discussion and the assertions set forth in Applicants' previous responses, Applicants respectfully submit that the rejections of the present claims under § 103 are completely unjustified, are not supported by any logical arguments or specific evidence of record, and are thus legally deficient. Applicants request that the present rejections of claims 22-24 be reconsidered and withdrawn.

Respectfully submitted,



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